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patient's anatomy and the target volumes to be irradiated, and further individualized after balancing possible benefits and risks that can be anticipated based on the outcome of treatment planning. Therefore, in agreement with the "Pareto principle", it is advisable to choose one basic treatment technique for the department that is most appropriate for 80% of the cases and select out of different other treatment setups in a highly individualized manner for the remaining 20% for which the basic treatment setup might not be optimal.
In the meantime, our knowledge about breast cancer and its' treatment continues to increase, leading to changing attitudes towards the selection of the most appropriate target volumes which might either be smaller like partial breast irradiation for low risk patients or quite more extended like comprehensive locoregional irradiation including the internal mammary lymph nodes for patients with adverse risk factors. At the same time, dose prescription will follow the outcome of prospective clinical trials with hypofractionation with daily doses below 3 Gy already widely introduced in daily clinical practice and with higher daily doses or dose variation over the target volumes depending on the risk of recurrences being investigated. This can only go hand in hand with a continuing improvement of treatment delivery with a more homogeneous dose distribution overall and if indicated an intended dose variation like in the simultaneous integrated boost technique for high risk volumes. For all of this, an optimal interdisciplinary collaboration between researchers, radiation oncologists, medical physicists and radiation therapists is obviously indispensable.

Teaching Lecture: Evaluating toxicity of new targeted drugs

SP-0199
Evaluating the toxicity of new targeted drugs in combination with radiotherapy

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The aim of this lecture is to provide the practicing radiation oncologist with an overview of radiotherapy practice in the era of molecularly targeted agents, focusing on issues of safety and toxicity when these modalities are delivered concurrently or in interdigitated fashion.
As more targeted agents are approved for the treatment of metastatic cancers, the challenge of managing these combinations in the palliative and oligometastatic settings, where the use of standard low- and SBRT dose range prescriptions are employed, respectively, is becoming increasingly common. An overview of available clinical data will be provided for classes of agents in common use, including inhibitors of the EGFR, VEGF and mTOR axes. Immunomodulatory agents and PARP inhibitors will also be discussed.
Design of clinical trials to evaluate combinations of targeted agents with radiotherapy also presents unique challenges. Issues regarding endpoint selection and DLT definition will be explored using data and illustrative examples. Alternative approaches of capturing toxicity data, e.g. from population databases will also be discussed.

Teaching Lecture: QA and commissioning of brachytherapy treatment planning systems

SP-0200
QA and commissioning of brachytherapy treatment planning systems

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Quality assurance and commissioning of brachytherapy treatment planning systems (TPS) comprise among other tasks verification of single and multiple source isodose distributions, applicator reconstruction, electronic data transfer, optimization software and dose volume histogram calculations. Comparison of TPS derived plans against a second TPS is valuable as is end-to-end dose measurements of plan delivery. While output by dose calculation engines based on the TG43 formalism is easy to verify, the task is more complex for the recently introduced model based dose calculations algorithms (MBDCA). The American Association of Physicists in Medicine (AAPM) has initiated a "Working Group on Model-Based Dose Calculation Algorithms in Brachytherapy" to derive and distribute well defined test plans and recommendations for commissioning MBDCAs. This lecture will cover existing recommendations for commissioning radiotherapy and in particular brachytherapy TPS, provide practical examples of the process and an update on the ongoing work to derive and distribute test plans for commissioning MBDCAs.

Teaching Lecture: Review of (low dose) radiotherapy for benign disease

SP-0201
Review of (low dose) radiotherapy for benign disease

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Abstract not received.

Symposium with Proffered Papers: Lung - treatment intensification and individualisation I

SP-0202
Pulmonary toxicity

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Purpose: Radiation induced pulmonary toxicity after radical radiotherapy or chemoradiation is difficult to score in lung cancer patients because tumor progression and exacerbation of preexisting pulmonary co-morbidities may have similar clinical characteristics. This presentation discusses several aspects of pulmonary toxicity.
A mild dry cough is common during the acute phase of lung irradiation. Radiation Pneumonitis (RP) is characterized by dyspnea, unproductive cough and occasionally mild fever, and typically presents between 1-6 months after treatment. Severe late lung complications, like pulmonary fibrosis,

hemorrhage, bronchial- or mainstem stenosis are relatively unusual and may develop beyond 4 years after treatment. Estimation of the probability to develop RP is important for patients with inoperable lung cancer. Studies of the risk of RP have used various dosimetric parameters like the Mean Lung Dose (MLD) or V20. To increase the sensitivity to predict RP, dosimetric and non-dosimetric factors can be combined. Palma et al (ref 1) performed a meta-analysis of both dosimetric and non-dosimetric factors based on individual patients treated with concurrent chemoradiation. The factors predicting RP were type of chemotherapy (carboplatin/paclitaxel vs cisplatin/etoposide or other chemotherapy), age, MLD and V20. Pre-existing radiological interstitial lung disease (ILD) findings were analyzed in a recent Japanese study of 157 patients and correlated with the incidence of RP after stereotactic body radiation therapy (SBRT) for stage I NSCLC (ref 2). Multivariate analysis identified ILD as risk factor for ≥ Gr2 RP, as well as the irradiated lung volume.

Recall radiation pneumonitis describes a rare reaction in previously irradiated lung tissue after application of triggering agents. Recall RP has been associated with multiple drugs such as taxanes, gemcitabine, vinca alkaloids, adriamycin and epirubicin. Tyrosine kinase inhibitors (erlotinib, cetuximab, sunitinib) have also been associated with recall RP and increased risk of severe RP following palliative or definitive radiation therapy. Some researchers have found a significant correlation between pulmonary toxicity and pre- and post radiation therapy pulmonary function tests. However, reduction in e.g. diffusion capacity varies widely between the grades of RP, making it less useful in routine clinical practice.

To improve the quality of lung toxicity reporting investigations of Patient Reported Outcome (PRO) tools are being developed. In literature discrepancies between patients and clinicians reported toxicity as well as low correlation with CTCAE scoring are reported. Generally clinicians tend to underreport the incidence and severity of symptoms. In a recently published analysis of lung cancer patients treated with radiotherapy/chemoradiation agreement ranged from slight to substantial (ref 3). These differences underline the significance of the introduction of PROs in clinical trials.

Summary: Dosimetric and clinical factors help us to estimate the incidence and severity of radiation induced pulmonary toxicity in clinical practice. In addition to these factors PROs tools on toxicity should be integrated in daily routine and in clinical trials to facilitate the doctors and patients decisions in the near future.

References:
1) Palma D et al, Int J Radiat Oncol Biol Phys. 2013 Feb 1;
2) Ueki N et al. J Thorac Oncol. 2014 Nov 6.
3) Christodoulou M et al. Radiother Oncol. 2014 Aug 5.

SP-0203

Dose / fractionation / IMRT / Imaging

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Radiotherapy (RT) plays a major role in the management of lung cancer as most patients are not surgical candidates due to stage, fitness and comorbidities. In the last decade we have witnessed tremendous changes in the role of radiation for the radical treatment of lung cancer as a result of the optimisation of chemo-radiotherapy combinations and technological advances.

The technology available for RT planning, delivery and verification of lung cancer treatment is evolving at a fast pace. Unfortunately the evidence to demonstrate the benefit of such technology in terms of toxicity, local control, survival or quality of life is limited.

Despite advances in the field of advanced RT techniques, local control with current RT doses delivered with standard 3D conformal RT is poor with local progression-free survival rates of about 30 %, even with concurrent CTRT. It is now well accepted that that improved local control in lung cancer can lead to improvement in survival [Aupérin A. J Clin Oncol 2010]. The following strategies can be combined to improve outcome in lung cancer include:

- Use of Intensity-modulated radiotherapy

IMRT is a technique that adds fluence modulation to beam shaping, which improves radiotherapy dose conformity around the tumour and spares surrounding normal structures. Treatment with IMRT is becoming more widely available for the treatment of lung cancer, despite the paucity of high level evidence supporting the routine use of this more resource intense and complex technique [Chan. JTO 2014]. It allows the treatment of patients with large volume disease, close to critical organs at risk with curative doses.

· Dose escalation

A clear radiation dose–response relationship exist in locally advanced NSCLC [Martel. Lung Cancer 1999]. The relationship between local control and BED is further suggested by data from SABR studies. The encouraging results of phase 1 and 2 dose studies conducted in the 1990s formed the basis for the RTOG 0617 study [Bradley. ASCO 2013]. In that 2 x 2 factorial design study, patients with stage III NSCLC were randomized to receive high dose (74 Gy in 37 fractions) or standard dose (60 Gy in 30 fractions) RT concurrently with weekly paclitaxel/carboplatin with or without cetuximab. Disappointingly, there was a significant increase in the risk of death in the high-dose arms (median survival, 19.5 months vs 28.7 months; p=0.0007), and a 37% increase in the risk of local failure in the high-dose arms (hazard ratio, 1.37; p=0.0319). There is therefore no role for dose escalation in stage III NSCLC using conventional dose fractionation

· Acceleration

Hyperfractionated and/or accelerated fractionating schedules have demonstrated superior survival compared to conventional fractionation at the expense of greater oesophageal toxicity [Mauguen JCO 2012]

· Dose redistribution based on functional imaging

Targeted dose escalation to tumour volumes resistant to treatment or at increased risk for recurrence is under evaluation [NCT01024829 and NCT01507428]

- Individualisation of the dose (concept of isotoxic RT)

The recognition of cancer heterogeneity has driven us away from the 'one size fits all' approach and has allowed tailoring of treatment to individualised patient-tumour characteristics. Isotoxic radiotherapy is a novel concept of personalised radiotherapy treatment allowing the individualised administration of radiotherapy dose based on predefined normal tissue constraints.

OC-0204

The first toxicity results of the PET-boost trial (NCT01024829)

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